Remarks

Claims 14-19 and 22-24 are pending. Claim 14 is currently amended. Support for the amendment can be found at, for example, paragraphs [0014]-[0025], [0028]-[0030], [0032], [0033] of the originally filed application. The Applicants respectfully request entry of the amendment to Claim 14 as the amendment is believed to place the application in better condition for allowance or, alternatively, appeal. Claims 14-19 and 22-24 are rejected.

The Applicants also wish to thank the Examiner, at the outset, for the withdrawal of the prior rejections made under 35 USC §102.

Claims 14-19 and 22-24 are rejected as not satisfying the written description of 35 USC §112, first paragraph. The rejection states the specification "*provides written description of antiCD20 antibodies such as rituximab which bind* ***human*** *CD20 for use in the claimed method.*"

Amended Claims 14-19 and 22-24 satisfy the written description requirement of 35 USC §112, first paragraph. The amended claims now recite "a monoclonal antibody directed against human transmembrane antigen CD20 of pre-B or mature lymphocytes[.]" The Applicants also note the amendments are consistent with the helpful guidance provided by the Examiner in the Official Action. Thus, the Applicants respectfully request the withdrawal of the rejections of amended Claims 14-19 and 22-24 under 35 USC §112, first paragraph.

Amended Claims 14-19 and 22-24 are rejected as obvious under 35 USC §103(a) over the combination of Wilson, US '137 and US '194.

Claims 14-19 and 22-24 are not obvious under 35 USC §103(a) over the combination of Wilson, US '137 and US '194. Reasons are set forth below.

First, the rejection states that Wilson discloses the treatment of MCL lymphoma patients with the anti-CD20 antibody RITUXIMAB™ and a therapeutic vaccination with a tumor idiotype. The rejection asserts that Wilson discloses a method to stimulate the T-cell response including tumor cell lysis, that Wilson teaches B-cell depletion can enhance the cellular immune response and that Wilson provides evidence in humans that treated patients have an enhanced cellular immune response. Thus, according to the rejection, the claimed methods would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. The rejection asserts this is because Wilson and US '137 teach that B-cell depletion can enhance the cellular immune response and

provides evidence in humans that treated patients have an enhanced cellular response while US '194 teaches the therapeutic vaccine recited in the claims.

The Applicants totally disagree with the arguments of the rejection.

This is because Wilson does not teach that B-cell depletion can enhance the cellular immune response. Indeed, the statement "but animal models suggest B-cell depletion may enhance cellular responses" in Wilson should be interpreted, not as enunciating a general principle, but should be interpreted in relation to the subject of the article which is MCL (mantle cell lymphoma). Thus, this statement should only be interpreted as meaning that in MCL patients with intact cellular immunity, B-cell depletion may enhance cellular responses. *See e.g.* Wilson (first sentence). This is also confirmed by the last statement in Wilson that "Id-KLH/GM-CSF vaccine can induce T-cell responses in most MCL patients following rituximab." *See* Wilson (last sentence) (emphasis added).

Second, nothing in Wilson would motivate one of ordinary skill in the art to apply the teachings of this reference, which are specific to MCL lymphoma patients with intact cellular immunity, to immune compromised HIV infected patients. Indeed, these two pathologies have nothing in common.

For example, it is well known that HIV AIDS patients do not have intact cellular immunity. Thus, while it is obvious to treat a B-cell lymphoma expressing CD20 in MCL patients with an anti-CD20 antibody to deplete these diseased B-cells, it is not obvious to treat HIV with an anti-CD20 antibody. This is also confirmed by the teachings of US '137 which relate to the use of anti-CD20 mAbs to treat B-cell lymphoma. Consequently, it is mere speculation which is unsupported by the teachings of the cited references, when the rejection concludes it would have been obvious for one of ordinary skill in the art to apply the teachings of Wilson to a HIV specific therapeutic method. Stated differently, one of ordinary skill in the art would not be motivated to combine the teachings of Wilson, US '137 and US '194 to arrive at the claimed methods or reasonably expect to be successful in so doing.

Third, Wilson never demonstrated an enhancement of the cellular immune response, but instead merely appears to show a persistence of the cellular immune response. Wilson actually only appears to show a decrease in $CD4^+$ cells, a maintained level of $CD8^+$ cells and a decrease in B-cells. Thus, in Wilson the cellular immune response is very weak, in spite of combining chemotherapy with RITUXIMAB™ teatment. These results showing a very weak cellular immune response would

not motivate one of ordinary skill in the art to combine idiotype vaccination and an anti-human CD20 mAb, such as RITUXIMAB™, together without chemotherapy.

Fourth, Wilson does not prove the persistence of the cellular immune response is related to the administration of RITUXIMAB™. This is because the cellular immune response observed is very weak and may have existed even without the administration of RITUXIMAB™. Importantly, nothing in Wilson demonstrates the persistence of the T-cell response observed is related to RITUXIMAB™. There is not even an experimental protocol taught in Wilson to help clarify the relationship between RITUXIMAB™ administration and the persistence of this cellular immune response. Instead, it appears such a relationship is merely wishful thinking on the part of the Wilson authors.

Thus, one of ordinary skill in the art would not have been motivated to combine the teachings of Wilson, US '137 and US '194 to arrive at the claimed methods or reasonably expect success on so doing. This is because Wilson merely appears to teach that B-cell depletion can enhance the cellular immune response in MCL patients with intact cellular immunity (*i.e.* patients with a B-cell lymphoma expressing CD20). Further, Wilson does not show an "enhancement" in the cellular immune response, but rather a mere persistence of cellular immunity. Wilson also does not show that this persistence is related to the administration of RITUXIMAB™.

Fifth, US '137 does nothing to cure the deficiencies of Wilson. In fact, US '137 corroborates the fact that one of ordinary skill in the art would not be motivated to apply the teachings of Wilson to the treatment of HIV. This is because US '137 relates, just as Wilson does, to the treatment of B-cell lymphoma (*i.e.* treatment of patients with a B-cell lymphoma expressing CD20).

Sixth, the citation of US '194 does nothing to cure the deficiencies of the core combination of Wilson and US '137. This is because US '194 does not describe, nor suggest, a composition comprising a human CD20 specific antibody or the claimed methods.

Last, the rejection points out that attorney argument cannot take the place of evidence. However, the Applicants respectfully submit that the arguments in the rejection are mere speculation made *a posteriori* based on knowledge of the application and claimed methods.

The Applicants respectfully request the withdrawal of the rejections of amended Claims 14-19 and 22-24 under 35 USC §103(a).

In light of the foregoing, the Applicants respectfully submit that the entire application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,

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